syndrome, Behcet syndrome, bites and stings, blood disorders including cold-haemagglutinin disease, haemolytic anemia, hypereosinophilia, hypoplastic anemia, macroglobulinaemia, trombocytopenic purpura, furthermore, for the management of bone disorders, cerebral oedema, Cogan's syndrome, congenital adrenal hyperplasia, connective tissue disorders including lichen, lupus erythematosus, polymyalgia rheumatica, polymyositis and dermatomyositis, epilepsy, eye disorders including cataracts, Graves' ophthalmopathy, haemangioma, herpes infections, neuropathies, retinal vasculitis, scleritis, for some gastro-intestinal disorders including inflammatory bowel disease, nausea and oesophageal damage, for hypercalcaemia, infections including of the eye, infections mononucleosis), for Kawasaki disease, myasthenia gravis, various pain syndromes including postherpetic neuralgia, for polyneuropathies, pancreatitis, in respiratory disorders including asthma, for the management of rheumatoid disease and osteoarthritis, rhinitis, sarcoidosis, skin diseases including alopecia, eczema, erythema multiforme, lichen, pemphigus and pemphigoid, psoriasis, pyoderma gangrenosum, and urticaria, in case of thyroid and vascular disorders.

REMARKS

This application is a continuation of International Application No. PCT/EP98/08421. Consideration of this application, as amended, is respectfully requested.

By virtue of this amendment, claims 8, 10, 15-20, 25, 42 and 43 have been canceled without prejudice. Claims 1-7, 9, 11-14, 21-24, 26-41 and 44-50 have been amended in order to conform the claims of the international application, as amended under Article 19 of the Patent Cooperation Treaty, to proper U.S. Patent and Trademark Office practice. Attached hereto is a marked-up version of the changes made to the claims and specification by the present amendment, entitled "Version of Claim Amendments With Markings to Show Changes Made."

Support for all claim amendments and all new claims is found in the specification as originally filed. No new matter has been added, and no new claims have been added.

Applicants believe that no fees are due as a result of this amendment. In the event of a fee discrepancy, please charge our Deposit Account No. 50-0552.

Respectfully submitted,

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VERSION OF CLAIM AMENDMENTS
WITH MARKINGS TO SHOW CHANGES MADE

Claims 1-7, 9, 11-14, 21-24, 26-41 and 44-50 have been amended as follows:

1. **(Amended)** A formulation comprising penetrants being capable of penetrating the pores of a barrier, even when the average diameter of said pores is smaller than the average diameter of said penetrants, **wherein said penetrants can transport agents or enable agent penetration through said pores after said penetrants have entered said pores,** wherein the formulation comprises

at least one consistency builder in an amount that increases the formulation viscosity above that of the non-thickened corresponding formulation to maximally 5 **[Nm/s]** **Ns/m^2** so that spreading over, and retention at, the application area is enabled **[and/or]** **, or**

at least one antioxidant in an amount that reduces the increase of oxidation index to less than 100 % per 6 months **[and/or]** **, or**

at least one microbicide in an amount that reduces the bacterial count of 1 million germs added per **[g]** **gram** of total mass of the formulation to less than 100 in the case of aerobic bacteria, to less than 10 in the case of entero-bacteria, and to less than 1 in the case of Pseudomonas aeruginosa or Staphilococcus aureus, after a period of 4 days.

2. **(Amended)** **[Formulation]** **The formulation** according to claim 1, **[characterised in that]** **wherein** said at least one consistency **[buildner]** **builder** is added in an amount that increases the formulation viscosity to up to 1 **[Nm/s and more preferably to up to 0.2 Nm/s]** **Ns/m^2**.

3. **(Amended)** **[Formulation]** **The formulation** according to claim 1 **[or 2, characterised in that]** **, wherein** said at least one antioxidant is added in an amount that reduces the increase of oxidation index to less than 100 % per 12 months **[and more preferably to less than 50 % per 12 months]**.

4. **(Amended)** **[Formulation]** **The formulation** according to **[any one of the preceding claims, characterised in that]** **claim 1, wherein** said at least one microbicide is added in an amount that reduces the bacterial count of 1 million germs added per **[g]** **gram** of total mass of the formulation to less than 100 in the case of aerobic bacteria, to less than 10 in the case of entero-bacteria, and to less than 1 in the case of Pseudomonas aeruginosa or Staphilococcus aureus, after a period of 3 days **[, and more preferably after a period of 1 day]**.

5. **(Amended)** **[Formulation]** **The formulation** according to **[any of the preceding claims, characterised in that]** **claim 1, wherein** the consistency builder is selected from **the group consisting of:**

pharmaceutically acceptable hydrophilic polymers, **[such as]** **including** partially etherified cellulose derivatives, comprising carboxymethyl -, hydroxyethyl-, hydroxypropyl-, hydroxypropylmethyl- or methyl-cellulose;

completely synthetic hydrophilic polymers **[comprising]** **including** polyacrylates, polymethacrylates, poly(hydroxyethyl)-, poly(hydroxypropyl)-, poly(hydroxypropylmethyl)methacrylate, polyacrylonitrile, methallyl-sulphonate, polyethylenes, polyoxiethylenes, polyethylene glycols, polyethylene glycol-lactide, polyethylene glycol-diacrylate, polyvinylpyrrolidone, polyvinyl alcohols, poly(propylmethacrylamide), poly(propylene fumarate-co-ethylene glycol), poloxamers, polyaspartamide, (hydrazine cross-linked) hyaluronic acid, silicone;

natural gums **[comprising]** **including** alginates, carrageenan, guar-gum, gelatine, tragacanth, (amidated) pectin, xanthan, chitosan collagen, agarose; **and**

mixtures and further derivatives or co-polymers thereof **[and/or other pharmaceutically, or at least biologically, acceptable polymers]**.

6. **(Amended)** **[Formulation]** **The formulation** according to claim 5, **[characterised in that]** **wherein** the polymer weight fractions are in the range between 0.05 % and 10% **[, more preferably are in the range between 0.1% and 5 %, even more preferably**

are in the range between 0.25 % and 3.5 % and most preferably are in the range between 0.5 % and 2 %].

7. **(Amended)** **[Formulation]** **The formulation** according to **[any one of the preceding claims, characterised in that]** **claim 1, wherein** the anti-oxidant is selected from **the group consisting of:**

synthetic phenolic antioxidants, **[such as]** **including** butylated hydroxyanisol (BHA), butylated hydroxytoluene (BHT) and di-tert-butylphenol (LY178002, LY256548, HWA-131, BF-389, CI-986, PD-127443, E-5119, BI-L-239XX), tertiary butylhydroquinone (TBHQ), propyl gallate (PG), 1-O-hexyl-2,3,5-trimethylhydroquinone (HTHQ);

aromatic amines, including diphenylamine, p-alkylthio-o-anisidine, ethylenediamine derivatives, carbazol and tetrahydroindenoindol;

phenols and phenolic acids, including guaiacol, hydroquinone, vanillin, gallic acids and their esters, protocatechuic acid, quinic acid, syringic acid, ellagic acid, salicylic acid, nordihydroguaiaretic acid (NDGA), eugenol;

tocopherols and their derivatives including tocopheryl-acylate, -laurate, myristate, -palmitate, -oleate,-linoleate, or any other suitable tocopheryl-lipoate, tocopheryl-POE-succinate;

trolox and corresponding amide and thiocarboxamide analogues;

ascorbic acid and its salts, isoascorbate, (2 or 3 or 6)-o-alkylascorbic acids, ascorbyl esters, including 6-o-lauroyl, myristoyl, palmitoyl-, oleoyl, or linoleoyl-L-ascorbic acid;

non-steroidal anti-inflammatory agents (NSAIDs), such as indomethacine, diclofenac, mefenamic acid, flufenamic acid, phenylbutazone, oxyphenbutazone acetylsalicylic acid, naproxen, diflunisal, ibuprofene, ketoprofene, piroxicam, penicillamine, penicillamine disulphide, primaquine, quinacrine, chloroquine, hydroxychloroquine, azathioprine, phenobarbital, acetaminephen;

aminosalicylic acids and derivatives;

methotrexate, probucol, antiarrhythmics, including amiodarone, aprindine, asocainol;

ambroxol, tamoxifene, b-hydroxytamoxifene;

calcium antagonists, including nifedipine, nisoldipine, nimodipine, nicardipine, nilvadipine, beta-receptor blockers including atenolol, propranolol and nebivolol;

sodium bisulphite, sodium metabisulphite, thiourea;

chellating agents, **[such as]** **including** EDTA, GDTA, desferral;

miscellaneous endogenous defence systems, **[such as]** **including** transferrin, lactoferrin, ferritin, cearuloplasmin, haptoglobion, haemopexin, albumin, glucose, ubiquinol-10;

enzymatic antioxidants, **[such as]** **including** superoxide dismutase and metal complexes with a similar activity, including catalase, glutathione peroxidase, and less complex molecules, **[such as]** **including** beta-carotene, bilirubin, uric acid;

flavonoids including flavones, flavonols, flavonones, flavanonals and chacones, anthocyanins;

N-acetylcystein, mesna, glutathione, thiohistidine derivatives, triazoles;

tannines, cinnamic acid, hydroxycinnamatic acids and their esters, including coumaric acids and esters, caffeic acid and their esters, ferulic acid, (iso-) chlorogenic acid, sinapic acid;

spice extracts, including spice extracts from clove, cinnamon, sage, rosemary, mace, oregano, allspice and nutmeg;

carnosic acid, carnosol, carsolic acid; rosmarinic acid, rosmaridiphenol, gentisic acid, ferulic acid;

oat flour extracts, **[such as]** **including** avenanthramide 1 and 2; thioethers, dithioethers, sulphoxides, tetralkylthiuram disulphides;

phytic acid, steroid derivatives, including U74006F; **and**

tryptophan metabolites, including 3-hydroxykynurenine and 3-hydroxyanthranilic acid, and organochalcogenides.

9. **(Amended)** **[Formulation]** **The formulation** according to **[any one of the preceding claims, characterised in that]** **claim 1, wherein** the microbicide is selected from **the group consisting of:**

short chain alcohols, **[comprising]** **including** ethyl and isopropyl alcohol, chlorbutanol, benzyl alcohol, chlorbenzyl alcohol, dichlorbenzylalcohol, hexachlorophene;

phenolic compounds, **[such as]** **including** cresol, 4-chloro-m-cresol, p-chloro-m-xylenol, dichlorophene, hexachlorophene, povidon-iodine;

parabenes, **[especially]** **including** alkyl-parabenes, **[such as]** **including** methyl-, ethyl-, propyl-, or butyl- paraben, benzyl paraben;

acids, **[such as]** **including** sorbic acid, benzoic acid and their salts;

quaternary ammonium compounds, **[such as]** **including** alkonium salts, **[e.g. a bromide,]** benzalkonium salts, **[such as]** **including** a chloride or a bromide, cetrimonium salts, **[e.g. a bromide,]** phenoalkecinium salts, **[such as]** **including** phenododecinium bromide, cetylpyridinium chloride and other salts;

mercurial compounds, **[such as]** **including** phenylmercuric acetate, borate, or nitrate, thiomersal, chlorhexidine or its gluconate, **[or any antibiotically active compounds of biological origin, or any mixture]** **and mixtures** thereof.

11. **(Amended)** **[Formulation]** **The formulation** comprising penetrants being capable of penetrating the pores of a barrier, even when the average diameter of said pores is smaller than the average diameter of said penetrants, **wherein said penetrants can transport agents or enable agent penetration through said pores after said penetrants have entered said pores,** the agents associated with said penetrants being corticosteroids, especially glucocorticoids or mineralocorticosteroids, **[characterised in that]** **wherein** the relative content of corticosteroids is above 0.1 weight-%, relative to total dry mass of the formulation.

12. **(Amended)** **[Formulation]** **The formulation** according to claim 11, **[characterised in that]** **further comprising** at least one consistency builder **[and/or]** **or** at least one anti-oxidant **[and/or]** **or** at least one microbicide **[according to any one of the claims 1 through to 10 is added to the formulation]** **and mixtures thereof**.

13. **(Amended)** **[Formulation]** **The formulation** according to claim 11 **[or 12, characterised in that]** **, wherein** the corticosteroid is selected from **the group consisting of:** alclonetasone dipropionate, amcinonide, beclomethasone dipropionate, betamethasone,

betamethasone 17-valerate, betamethasone 17,21-divalerate, betamethasone 21-acetate, betamethasone 21-buytrate, betamethasone 21-propionate, betamethasone 21-valerate, betamethasone benzoate, betamethasone dipropionate, betamethasone valerate, budesonide, clobetasol propionate, clobetasone butyrate, cortexolone, corticosterone, cortisone, cortisone 17-acetate, 21-deoxybetamethasone, 21-deoxybetamethasone 17-propionate, deoxycorticosterone, desonide, desoxymethasone, dexamethasone, diflorasone diacetate, diflucortolone valerate, fluclorolone acetonide, flumethasone pivalate, fluocinolone acetonide, fluocinonide, fluocortin butyl, fluocortolone , 9-alpha-fluorocortisone, 9-alpha-fluorohydrocortisone, 9-alpha-fluoroprednisolone, fluprednidene acetate, flurandrenolone, halcinonide, hydrocortisone, hydrocortisone 17-acetate, hydrocortisone 17-butyrate, hydrocortisone 17-propionate, hydro cortisone 17-valerate, hydrocortisone 21-acetate, hydrocortisone 21-butyrate, hydrocortisone 21-propionate, hydrocortisone 21-valerate, 17-alpha-hydroxyprogesterone, methylprednisolone acetate, mometasone furoate, prednisolone, prednisone, prednisone 17-acetate, prednisone 17-valerate, progesterone, triamcinolone, **and** triamcinolone acetonide.

14. **(Amended)** **[Formulation]** **The formulation** according to **[any one of the preceding claims, characterised in that]** **claim 1, wherein** the penetrants are suspended or dispersed in a polar liquid in the form of fluid droplets surrounded by a membrane-like coating of one or several layers, said coating comprising at least two kinds or forms of amphiphilic substances with a tendency to aggregate,

[provided that] **wherein** said at least two substances differ by at least a factor of 10 in solubility in said liquid or **[else that]** **wherein** said substances when in the form of homo-aggregates, for the more soluble substance, or of hetero-aggregates, for any combination of both said substances, have a preferred average diameter smaller than the diameter of the homo-aggregates containing merely the less soluble substance; or

[else provided that] **wherein** the presence of the more soluble substance lowers the average elastic energy of the membrane-like coating in the vicinity of thermal energy.

21. **(Amended)** **[Formulation]** **The formulation** according to **[any one of claims 14 to 20, characterised in that]** **claim 14, wherein** the average penetrant diameter is between 30 nm and 500 nm **[, preferably between 40 nm and 250 nm, even more preferably between 50 nm and 200 nm and most preferably between 60 nm and 150 nm]**.

22. **(Amended)** **[Formulation]** **The formulation** according to **[any one of claims 14 to 20, characterised in that]** **claim 14, wherein** the average diameter of the penetrant is 2 to 25 times bigger than the average diameter of the pores in the barrier **[, preferably between 2.25 and 15 times bigger, even more preferably between 2.5 and 8 times bigger and most preferably between 3 and 6 times bigger than said average pore diameter]**.

23. **(Amended)** **[Formulation]** **The formulation** according to **[any one of claims 14 to 20, characterised in that]** **claim 14, wherein** the dry weight of all carrier droplets in a formulation for the use on human or animal skin is 0.01 weight-% (w-%) to 40 w-% of total formulation mass **[, in particular between 0.1 w-% and 30 w-%, particularly preferably between 0.5 w-% and 20 w-%, and most preferably between 1 w-% and 10 w-%]**.

24. **(Amended)** **[Formulation]** **The formulation** according to **[any one of claims 14 to 20, characterised in that]** **claim 14, wherein** the dry weight of all carrier droplets in a formulation for the use on human or animal mucosa is 0.0001 w-% to 30 w-% of total formulation mass.

26. **(Amended)** A method for preparing a formulation for non-invasive application in vivo, according to **[any one of the preceding claims, characterised in that]** **claim 11, comprising forming** penetrants capable of associating **[and/or]** **or** incorporating said agent molecules **[are formed]** from at least one amphiphilic substance, at least one polar fluid, at least one edge-active substance or surfactant, at least one corticosteroid in an amount of more than 0.1 w-% based on total dry mass of the formulation, and **[, in case,]** other **[customary]** **pharmaceutically acceptable** ingredients **[, which together form said formulation]**.

27. **(Amended)** The method of claim 26, **[characterised in that]** **wherein** at least one edge-active substance or surfactant, at least one amphiphilic substance, at least one hydrophilic fluid and the agent are dissolved to form a solution and **[, if required,]** **optionally** are mixed separately, the resulting (partial) mixtures or solutions then being combined to subsequently induce, preferably by action of mechanical energy **[, such as]** **including** shaking, stirring, vibrating, homogenising, ultrasonication, shear, freezing and thawing, or filtration using convenient driving pressure, the formation of penetrants that associate with **[and/or]** **or** incorporate the agent.

28. **(Amended)** The method of **[claims 26 or 27, characterised in that]** **claim 26, wherein** said amphiphilic substances are either used as such, or dissolved in a physiologically compatible polar fluid, which may be water or miscible with water, or in a solvation-mediating agent, together with a polar solution.

29. **(Amended)** The method of **[claims 26 or 27, characterised in that]** **claim 26, wherein** said amphiphilic substances are dissolved in highly volatile alcohols **[, in especially ethanol,]** or in pharmaceutically acceptable organic solvents, which are then removed **[, esp. by evaporation,]** prior to making final preparation.

30. **(Amended)** The method as claimed in **[claims 28 or 29, characterised in that]** **claim 26, wherein** the polar solution contains at least one edge-active substance or surfactant.

31. **(Amended)** The method according to **[any one of claims 26 through to 30, characterised in that]** **claim 26, wherein** the formation of said penetrants is induced by the addition of required substances into a fluid phase, evaporation from a reverse phase, by injection or dialysis, if necessary under the influence of mechanical stress, **[such as]** **including** shaking, stirring, **[in especially high velocity stirring,]** vibrating, homogenising, ultrasonication,

shearing, freezing and thawing, or filtration using **[convenient, in especially]** low (1 MPa) or intermediate (up to 10 MPa)**[,]** driving pressure.

32. **(Amended)** The method of claim 31, **[characterised in that]** **wherein** the formation of said penetrants is induced by filtration, the filtering material having pores sizes between 0.01 µm and 0.8 µm **[, preferably between 0.02 µm and 0.3 µm, and most preferably between 0.05 µm and 0.15 µm, whereby several filters may be used sequentially or in parallel]**.

33. **(Amended)** The method according to **[any one of claims 26 through to 32, characterised in that]** **claim 26, further comprising associating** said agents and penetrants **[are made to associate]**, at least partly, after the formation of said penetrants, **[e.g. after]** **by** injecting a solution of the drug in a pharmaceutically acceptable fluid, **[such as]** **including** ethanol, 1-and 2-propanol, benzyl alcohol, propylene glycol, polyethylene glycol (molecular weight: 200 – 400 D) or glycerol, into the suspending medium, **wherein** said penetrants being formed previously, using the corresponding or some other suitable manufacturing method, or simultaneously with the drug injection, if required using a co-solution of the drug and, at least some, penetrant ingredients.

34. **(Amended)** The method according to **[any one of claims 26 through to 33, characterised in that]** **claim 26, wherein** said penetrants, with which the agent molecules are associated **[and/or]** **or** into which the agent is incorporated, are prepared just before the application of the formulation, if convenient from a suitable concentrate or a lyophylisate.

35. **(Amended)** **[Formulation]** **The formulation** according to **[any one of claims 11 through to 25, characterised in that]** **claim 11, wherein** the content of corticosteroids is between 0.1 w-% and 20 w-% **[, more preferably between 0.25 w-% and 10 w-% and even more preferably between 0.5 w-% and 5 w-%, relative to total dry mass of drug-loaded carriers]**.

36. **(Amended)** **[Formulation]** **The formulation** according to claim 35, **[characterised in that]** **wherein** the relative content of corticosteroids in the case of triamcinolone or one of its derivatives, such as acetonide, is below 2 w-%, relative to total dry mass of the drug-loaded carriers **[, even more preferably is below 1 w-% and most preferably is below 0.5 w-%]**.

37. **(Amended)** **[Formulation]** **The formulation** according to claim **[35, characterised in that]** **36, wherein** the relative content of corticosteroids in the case of hydrocortisone or one of its derivatives is below 20 w-%, relative to total dry mass of the drug-loaded carriers **[, even more preferably is below 12.5 w-% and most preferably is below 5 w-%]**.

38. **(Amended)** **[Formulation]** **The formulation** according to claim 35, **[characterised in that]** **wherein** the relative content of corticosteroids in the case of dexamethasone or one of its derivatives is below 15 w-%, relative to total dry mass of the drug-loaded carriers **[, even more preferably is below 10 w-% and most preferably is below 5 w-%]**.

39. **(Amended)** **[Formulation]** **The formulation** according to claim 35, **[characterised in that]** **wherein** the relative content of corticosteroids in the case of clobetasol or one of its derivatives, such as propionate is below 15 w-%, relative to total dry mass of the drug-loaded carriers **[, even more preferably is below 10 w-% and most preferably is below 5 w-%]**.

40. **(Amended)** **[Formulation]** **The formulation** according to **[claims 35 to 39, characterised in that]** **claim 35, wherein** the content of said corticosteroid is below the saturation maximum, defined as the content of corticosteroid at which the corticosteroid begins to crystallise in or outside the carrier.

41. **(Amended)** **[Formulation]** <u>**The formulation**</u> according to **[claims 1 through to 25 and 35 through to 38, characterised in that]** <u>**claim 1, wherein**</u> in order to speed up drug action a permeation enhancer is added.

44. **(Amended)** **[Formulation]** <u>**The formulation**</u> according to **[claims 11 through to 25 and 35 through to 43, characterised in that]** <u>**claim 11, wherein**</u> said corticosteroid is added in an amount which enables the formulation to be applied corresponding to an area dose, as expressed by the total dry mass of penetrant applied per unit area, of between 0.1 mg cm^{-2} and 15 mg cm^{-2}, **[more preferably between 0.5 mg cm^{-2} and 10 mg cm^{-2}, particularly preferably between 0.75 mg cm^{-2} and 5 mg cm^{-2} and most preferably between 1 mg cm^{-2} and 2.5 mg cm^{-2},]** if said corticosteroid is desired to exert a therapeutic effect in the deep subcutaneous **[, e.g. muscle or joints,]** tissue or **[else in]** the remote tissues, including the whole body.

45. **(Amended)** **[Formulation]** <u>**The formulation**</u> according to **[claims 11 through to 25 and 35 through to 43, characterised in that]** <u>**claim 11, wherein**</u> said corticosteroid is added in an amount which enables the formulation to be applied with an area dose, as expressed by the total dry mass of penetrant applied per unit area, of **[1]** between <u>**1**</u> µg cm^{-2} and 250 µg cm^{-2}, **[more preferably between 2.5 and 100 µg cm^{-2}, even more preferably between 5 µg cm^{-2} and 50 µg cm^{-2} and most preferably between 7.5 µg cm^{-2} and 20 µg cm^{-2},]** if said corticosteroid is desired to exert a mainly local **[, that is, superficial,]** rather than systemic therapeutic effect.

46. **(Amended)** **[Formulation]** <u>**The formulation**</u> according to **[claims 11 through to 25 and 35 through to 45, characterised in that]** <u>**claim 11, wherein**</u> consistency and, if necessary other characteristics of the formulation are appropriately selected to enable spraying, smearing, rolling or sponging of the formulation on the application area in particular by using a sprayer, spender, roller or sponge **[, as appropriate]**.

47. **(Amended)** A method for non-invasive application of corticosteroids by means of penetrants according to **[any one of the preceding claims, characterised in that]** **claim 1, wherein** the area dose, as expressed by the total dry mass of penetrant applied per unit area, is selected to be between 0.1 mg cm^{-2} and 15 mg cm^{-2}, **[preferably between 0.5 mg cm^{-2} and 10 mg cm^{-2}, particularly preferably between 0.75 mg cm^{-2} and 5 mg cm^{-2} and most preferably between 1 mg cm^{-2} and 2.5 mg cm^{-2},]** if said corticosteroid is desired to exert a therapeutic effect in the deep subcutaneous **[, e.g. muscle or joints,]** tissue or **[else in]** the remote tissues, including the whole body.

48. **(Amended)** A method for non-invasive application of corticosteroids by means of penetrants according to **[any one of the preceding claims, characterised in that]** **claim 1, wherein** the area-dose, as expressed by the total dry mass of penetrants applied per unit area, is between 1 µg cm^{-2} and 250 µg cm^{-2}, **[preferably between 2.5 µg cm^{-2} and 100 µg cm^{-2}, more preferably between 5 µg cm^{-2} and 50 µg cm^{-2} and most preferably between 7.5 µg cm^{-2} and 20 µg cm^{-2},]** if said corticosteroid is desired to exert a mainly local **[, that is, superficial,]** rather than systemic therapeutic effect.

49. **(Amended)** A method for non-invasive application of corticosteroids associated with or encapsulated into said penetrants according to **[any one of the preceding claims, characterised in that]** **claim 1, wherein** the formulation is applied by spraying, smearing, rolling or sponging on the application area in particular by using a sprayer, spender, roller or sponge **[, as appropriate]**.

50. **(Amended)** Use of a formulation in accordance with **[any one of the preceding claims]** **claim 1** for the treatment of inflammatory disease, dermatosis, kidney or liver failure, adrenal insufficiency, aspiration syndrome, Behcet syndrome, bites and stings, blood disorders **[, such as]** **including** cold-haemagglutinin disease, haemolytic anemia, hypereosinophilia, hypoplastic anemia, macroglobulinaemia, trombocytopenic purpura, furthermore, for the management of bone disorders, cerebral oedema, Cogan´s syndrome,

congenital adrenal hyperplasia, connective tissue disorders **[, such as]** **including** lichen, lupus erythematosus, polymyalgia rheumatica, polymyositis and dermatomyositis, epilepsy, eye disorders **[, such as]** **including** cataracts, Graves´ophthalmopathy, haemangioma, herpes infections, neuropathies, retinal vasculitis, scleritis, for some gastro-intestinal disorders **[, such as]** **including** inflammatory bowel disease, nausea and oesophageal damage, for hypercalcaemia, infections **[, e.g.]** **including** of the eye **[(as in)** , infections mononucleosis), for Kawasaki disease, myasthenia gravis, various pain syndromes **[, such as]** **including** postherpetic neuralgia, for polyneuropathies, pancreatitis, in respiratory disorders **[, such as]** **including** asthma, for the management of rheumatoid disease and osteoarthritis, rhinitis, sarcoidosis, skin diseases **[, such as]** **including** alopecia, eczema, erythema multiforme, lichen, pemphigus and pemphigoid, psoriasis, pyoderma gangrenosum, **and** urticaria, in case of thyroid and vascular disorders.